UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION **This Document Relates to the TPP Trial Subclasses**	MDL No. 2875 Honorable Robert B. Kugler, District Court Judge

ZHP DEFENDANTS' REPLY IN SUPPORT OF MOTION TO AMEND OR CORRECT THE COURT'S OPINION ON THE PARTIES' LIABILITY EXPERTS AND OPPOSITION TO PLAINTIFFS' CROSS-MOTION TO EXCLUDE DR. AFNAN'S OPINIONS THAT RELY ON DR. XUE'S EXCLUDED OPINIONS

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INTRODUCTION

Plaintiffs' opposition fails to demonstrate why different parties should be subject to different rules in this litigation, and their effort to obtain a "second bite at the apple" with respect to their *Daubert* arguments in the form of a cross-motion is meritless and should be denied.

First, plaintiffs do not meaningfully address, much less refute, that the Court's rulings with respect to the types of regulatory opinions that may be offered by the parties' respective experts are inherently contradictory. Nor do plaintiffs address the legion of caselaw highlighting why regulatory experts like Dr. Afnan are not offering legal opinions when they explain complex regulatory schemes to the jury. Moreover, plaintiffs barely address the key issue raised by the ZHP defendants' motion: if Dr. Afnan's opinions regarding defendants' compliance with certain regulatory standards constitute inadmissible "legal opinions," then the same is true of plaintiffs' experts' opinions that the VCDs did not comply with those same standards.

Second, the Court should reject plaintiffs' attempt to relitigate challenges to the admissibility of Dr. Afnan's testimony that were already made to—and correctly rejected by—the Court. A significant portion of the "cross-motion" submitted by plaintiffs is nearly identical to their prior motion to exclude Dr. Afnan's opinions. Indeed, the very first argument in plaintiffs' initial motion to exclude Dr. Afnan was that he was unqualified to offer certain opinions that they described as relating to

chemistry. Plaintiffs simply repeat that assertion in their latest filing, even though the Court previously refused to exclude Dr. Afnan on that ground. Further, plaintiffs blatantly misrepresent Dr. Afnan's opinions as being based solely on the opinions of Dr. Fengtian Xue, which were excluded. In reality, Dr. Afnan's opinions are properly and reliably based on his Ph.D. in chemistry, hands-on work serving as a regulator for the FDA, decades of experience working in the pharmaceutical industry, and his fulsome review of the regulatory record in this case.

Accordingly, the ZHP defendants' motion should be granted and plaintiffs' cross-motion denied.

I. PLAINTIFFS CANNOT REFUTE THAT THE COURT INCORRECTLY TREATED THE OPINIONS OF DR. AFNAN DIFFERENTLY FROM THE OPINIONS OF PLAINTIFFS' EXPERTS.

As an initial matter, the portion of plaintiffs' filing that actually addresses the ZHP defendants' motion to amend or correct the Court's *Daubert* rulings is unpersuasive. First, plaintiffs fail to refute the long line of authorities recognizing that opinions like Dr. Afnan's regarding regulatory compliance are the appropriate subject of expert testimony, not improper legal opinions. And second, even if Dr. Afnan's opinions regarding compliance with regulatory standards could be properly characterized as "legal," the same would be true of the opinions of plaintiffs' experts regarding non-compliance with those same standards.

First, plaintiffs do not address, much less make any effort to distinguish, the countless authorities cited by the ZHP Defendants making clear that regulatory experts such as Dr. Afnan can explain complex regulatory schemes to a jury without providing legal opinions. (*See* Defs.' Mot. at 8-9 (demonstrating that courts both within this Circuit and around the country "allow[] FDA regulatory experts to testify regarding regulatory requirements") (citation omitted).) *See also, e.g.*, *In re Suboxone (Buprenorphine Hydrochloride & Naloxone) Antitrust Litig.*, No. 13-MD-2445, 2020 WL 6887885, at *45 (E.D. Pa. Nov. 24, 2020) (noting that "courts have repeatedly allowed FDA regulatory experts to testify regarding regulatory requirements"). Moreover, plaintiffs are unable to point to even one case in which a court precluded a regulatory expert from offering similar opinions regarding the meaning of, or a party's compliance with, regulatory standards on the grounds that they are legal opinions—likely because such a case would apply equally to their own experts. Nor did the Court cite any such law in its opinion. (*See* ECF 2581 at 5-7.) In short, plaintiffs' entire opposition to the ZHP Defendants' motion is not grounded in the law, and their arguments should be rejected for that reason alone.

Second, plaintiffs are unable to demonstrate that Dr. Afnan's excluded opinions are different in character from the regulatory opinions of a number of plaintiffs' witnesses whose opinions were not excluded. Dr. Afnan and Drs. Najafi and Plunkett all seek to offer opinions as to whether the VCDs were adulterated, and

whether they are therapeutically equivalent and bioequivalent to the RLD, Diovan, which require the interpretation and application of regulatory standards. (*See* Defs.' Mot. at 6-8.) If Dr. Afnan's opinion that the VCDs were not adulterated based on a review of the applicable regulatory standards is a "legal opinion[]"—which this Court has deemed it to be (*see* ECF 2581 at 6)—then Drs. Najafi and Plunkett coming to the opposite conclusion are legal opinions as well.

Plaintiffs make little effort to explain why the regulatory opinions offered by Drs. Plunkett and Najafi are not "legal opinions." Instead, plaintiffs assert that these experts have stronger bases for reaching their conclusions that regulatory standards were not met than Dr. Afnan does in opining that those same standards were satisfied. (*See* Pls.' Br. at 2-9 (plaintiffs contrasting the purportedly unreliable ***bases*** of Dr. Afnan's opinions to those of Drs. Najafi and Plunkett, who plaintiffs claim "built their opinions on a reliable foundation").) But this argument is unrelated to whether the regulatory opinions offered constitute "legal opinions." Regardless of the experts' "bases" for concluding that regulatory standards were or were not met, either all of these opinions are "legal opinions" or none of them is.

Apparently aware of this problem, plaintiffs attempt to rewrite the Court's *Daubert* ruling with respect to the bases for its exclusion of certain of Dr. Afnan's opinions. For example, plaintiffs assert that the Court excluded Dr. Afnan's opinion that "Prinston's drug products . . . continue to be considered therapeutically

equivalent" to Diovan since "[t]here is no reliable basis or methodology to support this opinion" but properly admitted Drs. Najafi and Plunkett's opinions "defin[ing] therapeutic equivalence and explain[ing] why [d]efendants' VCDs fail to meet that definition." (Pls.' Br. at 6-7 (citation omitted).) But, in reality, the Court excluded Dr. Afnan's opinion on this point because it purportedly "cross[ed] over into ***legal opinions***." (ECF 2581 at 6 (emphasis added).) If that were the case, then Dr. Najafi and Dr. Plunkett's opinions, regardless of their purported bases, should be excluded for the same reason.

Similarly, plaintiffs argue that the Court excluded Dr. Afnan's opinion that "[p]laintiffs' experts lack support for the assertion that generic valsartan API was not adulterated at the time of sale" because it was an "***obviously inaccurate*** legal opinion," whereas "[p]laintiffs' experts did not approach the issue [of adulteration in] the same flawed way." (Pls.' Br. at 7-8 (emphasis added) (citation omitted).) But this reasoning is illogical. Even if Dr. Afnan's opinion on adulteration were an inaccurate "legal opinion"—as plaintiffs insist—then Drs. Najafi and Plunkett's opinions on adulteration that are directly to the contrary would also be "legal opinions." For these reasons, treating plaintiffs' and defendants' regulatory experts' opinions on the exact same subject differently was erroneous. *See, e.g.*, *Breidor v. Sears, Roebuck & Co.*, 722 F.2d 1134, 1141 (3d Cir. 1983) (court "abused its discretion when it excluded" expert's testimony where without the expert's

"testimony plaintiffs were at a substantial disadvantage in countering the defendant's experts' testimony" on the same topic).

II. THE COURT SHOULD DENY PLAINTIFFS' SO-CALLED "CROSS-MOTION," WHICH ATTEMPTS TO IMPROPERLY AND BELATEDLY SUPPLEMENT REJECTED *DAUBERT* ARGUMENTS.

The Court should also reject plaintiffs' attempt to re-litigate their prior motion to exclude Dr. Afnan, which the Court denied in part, by recasting their opposition as a "cross-motion." According to plaintiffs, "***all*** of Dr. Afnan's substantive opinions," the overwhelming majority of which relate to regulatory and cGMP issues stemming from his experience as an FDA regulator and in the pharmaceutical industry, are somehow based on the chemistry opinions of Dr. Xue that have been excluded. (Pls.' Br. at 10-20 (emphasis added).) This argument should be rejected because: (1) plaintiffs already had their opportunity to challenge Dr. Afnan's opinions and the Court rejected this argument at that time; (2) Dr. Afnan's regulatory opinions do not turn on the chemistry opinions of Dr. Xue; and (3) to the extent Dr. Afnan did take into account Dr. Xue's opinions—i.e., with respect to the meaning of the July, 2017 Jinsheng Lin email—the record is clear that Dr. Xue's opinions informed Dr. Afnan's reading of the document, but did not provide the entire basis for Dr. Afnan's opinions with respect to it.

A. The Court Already Considered, And Rejected, Plaintiffs' Arguments.

The Court already considered many of the arguments in plaintiffs' cross-motion. The very first argument in plaintiffs' motion to exclude Dr. Afnan's testimony was that Dr, Afnan is not qualified to opine on issues related to chemistry, despite his Ph.D. in the subject and long tenure in the pharmaceutical industry evaluating chemical manufacturing processes. (*See* ECF 2286-1 at 14.) Specifically, plaintiffs argued in their *Daubert* briefing that "Dr. Afnan is not qualified to provide chemistry or toxicology opinions" (ECF 2286-1 at 14 (capitalization altered); *see also* ECF 2355 at 1-2), and that "if Dr. Xue's opinion" on "whether the reactions at issue could have been identified as possibilities . . . is precluded, any opinion formed in reliance on that opinion" by Dr. Afnan would also be precluded. (ECF 2286-1 at 28.) In addition, ***multiple pages*** of plaintiffs' "cross-motion" are essentially copied and pasted from their original motion. (*Compare, e.g.*, ECF 2286-1 at 29-30 ("Moreover, when confronted with the clear language of the July 27, 2017 email . . ."), *with* Pls.' Br. at 18-20 ("Moreover, when confronted with the clear language of the July 27, 2017 email . . ."); ECF 2286-1 at 3, *with* Pls.' Br. at 16.) The Court implicitly rejected those arguments when it permitted the majority of Dr. Afnan's testimony despite excluding Dr. Xue's substantive opinions. (*See* ECF 2581 at 5-7, 17-18.) Accordingly, this Court has already considered plaintiffs' arguments

on this score, and plaintiffs are not entitled to reargue them, long after the time for *Daubert* motions has passed, under the guise of a "cross-motion."

B. The Admissibility Of Dr. Xue's Opinions Has No Bearing On The Vast Majority Of Dr. Afnan's Opinions.

Plaintiffs' attempt to portray Dr. Afnan's ***regulatory*** opinions as being wholly based on the ***chemistry*** opinions of Dr. Xue should also be rejected since it is clear that his opinions are actually based on his own independent expertise and several other sources of evidence in the record, not Dr. Xue's opinions. *See Gagnon v. Lemoyne Sleeper Co.*, No. 1:CV-05-2081, 2009 WL 1324141, at *3, *7 (M.D. Pa. May 12, 2009) (rejecting argument that experts "did not have enough information to form an expert opinion" and that they were "only parroting the inadmissible opinions" of treating physicians where "the trial depositions of [the experts] thoroughly demonstrate[d] that their testimonies and expert opinions [were] based on much more than the reports and opinions of" the other physicians).

As explained above, Dr. Afnan is a regulatory expert who has spent decades working in both the pharmaceutical industry and at the FDA, and he has a Ph.D. in chemistry. (*See* Am. Rep. of Ali Afnan, Ph.D. ("Afnan Rep.") ¶¶ 2-11, Jan. 11, 2023 (Pls.' Br. Ex. 1); *see also* Dep. of Ali Afnan, Ph.D. ("Afnan Dep.") 158:3-13, Feb. 8, 2023 (Pls.' Br. Ex. 2) (Dr. Afnan explaining that he does "have a degree" and Ph.D. in chemistry," so he "understand[s] sufficiently about chemistry to opine on the subject").) In reaching his opinions, Dr. Afnan reviewed and relied upon a variety

of materials, including internal ZHP documents, fact witness depositions, scientific literature, FDA and other national and international regulatory rules and guidance, and the reports and depositions of other expert witnesses. (*See* Afnan Rep., App. B (Materials Reviewed & Considered (Amended & Supplemental)) (ECF 2324-2).) Further, only two of the 212 paragraphs that make up Dr. Afnan's report reference or cite to Dr. Xue. (*See* Afnan Rep. ¶¶ 141, 190.) Thus, plaintiffs' assertion that "all of Dr. Afnan's substantive opinions" are based on excluded testimony about chemistry from Dr. Xue strains credulity. (Pls.' Br. at 10.)

A few examples make this point even clearer.

First, plaintiffs argue that Dr. Afnan's opinions regarding the regulatory scheme and standards under which ZHP operated are based on Dr. Xue, including Dr. Afnan's purely regulatory opinions that: (1) "[n]ewer information not available while a product was on the market cannot retroactively render a product adulterated" (Pls.' Br. at 14 (citation omitted)); (2) "compliance with CGMPs turns on what is reasonably known at the time product manufacturing takes place" (*id.* at 13 (citation omitted)); and (3) the meaning of the phrase "potential impact" as used by the FDA in a Form 483 letter (*id.* at 14 (citation omitted)). But Dr. Afnan does not cite to or mention Dr. Xue in offering these opinions, which are well within his area of regulatory expertise.

Second, plaintiffs' argument that Dr. Afnan "extensive[ly] reli[ed]" on Dr. Xue's chemistry opinions in forming opinions regarding whether the potential formation of nitrosamines should have been expected prior to the recall significantly misrepresents Dr. Afnan's opinions and the bases for them. (Pls.' Br. at 15; *see also id.* at 12-14.) For example:

- Plaintiffs assert that Dr. Afnan opines that "neither industry nor regulators were aware that NDMA or NDEA could form" in the manufacturing processes based on Dr. Xue's excluded opinions about the reasonableness of ZHP's analyses of those process from the perspective of a chemist. (Pls.' Br. at 12 (quoting Afnan Rep. ¶ 135).) In truth, Dr. Afnan's opinions are premised on his expert interpretation of the "***FDA's*** findings that neither regulators nor industry," including official FDA statements that "neither regulators nor industry fully understood how NDMA or NDEA could form during this particular manufacturing process" prior to the 2018 recall. (Afnan Rep. ¶¶ 120-133.)

- Plaintiffs' assertion that Dr. Afnan's opinion that "there had been no literature indicating that NDMA was a potential impurity in valsartan API prior to June 2018" is based on Dr. Xue's report (Pls.' Br. at 13 (citation omitted)) is also baseless. Dr. Afnan makes that statement in connection with analyzing ZHP's deviation investigation report and does not reference Dr. Xue at all. (*See* Afnan Rep. ¶ 176 (citing ZHP00007221).)

- Plaintiffs also assert that Dr. Afnan's opinion that "[r]easonably expected impurities [in valsartan API] would not include NDMA or NDEA" is based on Dr. Xue's testimony. (Pls.' Br. at 13 (citation omitted).) But Dr. Afnan's report is clear that this statement is based on statements "by the FDA and other scientists." (Afnan Rep. ¶ 181; *see also id.* ¶¶ 120-133 (citing several FDA statements supporting that opinion).)

- There is also no truth to plaintiffs' argument that the "only concrete, non-conclusory basis" for Dr. Afnan's opinion that "ZHP performed lengthy, thorough investigations of these processes before submitting the manufacturing changes to the FDA" is Dr. Xue. (Pls.' Br. at 12-13 (citation omitted).) Dr. Afnan spends a significant portion of his report detailing the steps ZHP took prior to submitting its Drug Master File amendments based on the company's regulatory filings and documents—all without once relying on the opinions of Dr. Xue. (*See* Afnan Rep. ¶¶ 73-82.)

Further, even the portions of Dr. Afnan's report that do reference Dr. Xue are not supported solely by Dr. Xue's opinions. For example, plaintiffs claim that Dr. Afnan's citation to Dr. Xue's now-excluded opinions in Paragraph 141, "which present the overarching core of Dr. Afnan's opinions regarding ZHP's compliance with cGMPs and other regulatory obligations," dooms his opinion that ZHP did not have reason to expect that NDMA or NDEA could form here. (Pls.' Br. at 11.) But the immediately following paragraphs belie that Dr. Afnan was ever relying solely on Dr. Xue in coming to that opinion. As Dr. Afnan explains, that opinion is also supported by his own review of ZHP's risk assessment and the FDA's reaction to it, including that the ***FDA itself*** "never expressed any concerns regarding the processes . . . let alone concern that either process might lead to the formation of nitrosamines." (Afnan Rep. ¶ 142; *see also id.* ¶ 181 ("[A]s expressly acknowledged by the FDA and other scientists, such impurities were not expected to be present in

valsartan API or produced by the processes at issue.").) To suggest that such opinions are based wholly on Dr. Xue's opinions simply ignores the record.

In short, a cursory analysis of the opinions in Dr. Afnan's report belies plaintiffs' claim that he "extensively reli[ed]" on Dr. Xue.

Third, plaintiffs' argument that Dr. Afnan's criticisms of Drs. Hecht and Najafi are premised entirely on Dr. Xue's excluded opinions is also meritless. According to plaintiffs, Dr. Afnan could only critique these plaintiffs' experts' opinions "by relying on Dr. Xue's now excluded chemistry opinions." (Pls.' Br. at 14-15.) But this, too, is belied by the contents of Dr. Afnan's report. For example, Paragraph 146 of Dr. Afnan's report, which plaintiffs cite as an example of his purported reliance on Dr. Xue to critique Dr. Hecht (*id*. at 15), makes clear that it is the ***FDA's*** lack of concern about nitrosamines in valsartan, not Dr. Xue's opinions, on which he is basing his criticism of Dr. Hecht's opinions that the risks of nitrosamine formation were well known in the chemistry community at the time the recalled valsartan was being sold. (*See* Afnan Rep. ¶ 146 ("If Dr. Najafi and [p]laintiffs' other experts were correct that ZHP chemists should have known to test for NDMA in valsartan API based solely on the use of DMF, ***FDA chemists*** would have known this as well and raised a concern about it. They did not.") (emphasis added).) Similarly, in Paragraph 202 of his report, Dr. Afnan explains that his criticisms of Dr. Najafi's opinions are based on regulatory documents and the FDA's

public statements regarding its own (and the industry's) lack of knowledge regarding the potential for nitrosamine formation—not anything Dr. Xue said. (*Id.* ¶ 202.)

Fourth, there is no truth to plaintiffs' argument that Dr. Afnan "conceded his extensive reliance on Dr. Xue" for all of his opinions at his deposition. (Pls.' Br. at 15.) While plaintiffs point to carefully selected portions of Dr. Afnan's deposition answers as supposed evidence that Dr. Afnan based his entire report on Dr. Xue, the reality is to the contrary. Dr. Afnan testified that even those few opinions he offers that are based in part on Dr. Xue's are also premised on his own knowledge as a scientist with a Ph.D. in chemistry, his experience, and his expert review of the relevant materials. For example, with respect to whether he considered that DMF could degrade into DMA via either hydrolysis or thermal impact in forming his opinions about the case, Dr. Afnan explained that he conducted his own analysis and did not blindly rely on Dr. Xue:

> Q. Did you form your own independent opinion about what you just told me, or were you relying on Dr. Xue's analysis of that subject matter?
> A. Dr. Xue refers to two statements. One is about the boiling point of DMF, which I have referenced him and verified by looking at, effectively, the boiling point of DMF. I've also looked at the pH of the process, which, again, he refers to, and, again, I have verified.
> ***So is it my opinion or is it his opinion? It's my opinion.***

(Afnan Dep. 157:2-15 (cited except for emphasized portion in Pls.' Br. at 15).)

In short, Dr. Afnan's opinions are based on his own independent review of the record through the lens of his significant qualifications and expertise—not Dr. Xue's.

C. Dr. Afnan's Opinions Regarding The July 27, 2017 Email Are Not Based Exclusively On Dr. Xue's Interpretation Of The Document.

Finally, plaintiffs are also incorrect that Dr. Afnan's interpretation of the July 2017 email from Jinsheng Lin is based entirely on the opinions of Dr. Xue. (*See* Pls.' Br. at 11, 16-17.) Dr. Afnan explained in his deposition (outside of plaintiffs' cherry-picked quotes) that he did refer to Dr. Xue's reading of the July, 2017 email in his report but also independently "verified" that interpretation by applying his own expertise in reviewing "Ms. Jucai Ge's testimony on the subject," and reading translations of the email itself. (Afnan Dep. 205:16-206:7; *see also, e.g.*, *id.* 206:22-207:1 ("As I said, I verified by reading Jucai Ge's testimony where she is questioned extensively about the e-mail."); *id.* 207:8-20 (Dr. Afnan confirming through repeated questioning that he is "putting the most weight on . . . Jucai Ge's testimony"); *id.* 215:22-216:6 (Dr. Afnan confirming he is relying on Ms. Ge's deposition "[a]nd the text of the translated text, as well as the attachment that it refers to").)[1]

[1] To the extent plaintiffs assert that Dr. Afnan cannot rely on Jucai Ge's or other witnesses' testimony because it is "inadmissible hearsay" that is unreliable (*see* Pls.' *(cont'd)*

Based on that review—rather than blind reliance on Dr. Xue's opinions—Dr. Afnan determined that the email was about "Impurity K" and the "irbesartan process" and therefore is "not talking about NDMA." (Afnan Dep. 219:5-15; *see also id.* 245:14-246:18.) Plaintiffs may disagree with both the testimony of Ms. Ge—a native Chinese speaker who actually spoke with the author of the email—and Dr. Afnan's informed reading of the email, but Dr. Afnan is "permitted to base his opinion on a particular version of disputed facts and the weight to be accorded to that opinion is for the jury." *Walker v. Gordon*, 46 F. App'x 691, 695-96 (3d Cir. 2002); *see also MCI Commc'ns Serv. Inc. v. KC Trucking & Equip. LLC*, 403 F. Supp. 3d 548, 553, 556-57 (W.D. La. 2019) (rejecting argument that defendants' opinion "d[id] not have a basis or reason" since even "reliance on shaky evidence speaks to the weight of the evidence rather than admissibility").

CONCLUSION

For the foregoing reasons, the ZHP Defendants respectfully request that the Court amend or correct its ruling on the parties' liability experts to allow defendants' experts to offer opinions of the same kind and character as plaintiffs' experts and deny plaintiffs' cross-motion to exclude Dr. Afnan's opinions.

Br. at 17-18), it is axiomatic that the facts and data upon which an expert rely "need not be admissible for the opinion to be admitted," Fed. R. Evid. 703.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on February 20, 2024, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system, which will send a notice of electronic filing to all CM/ECF participants in this matter.

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